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☐ Initial submission ☐ Revised version ☒ Final submission

Life Sciences Reporting Summary

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Experimental design

1. Sample size

Describe how sample size was determined.

The number of samples and replicate runs were chosen to demonstrate the proof-of-principle for the CMOS biochip technology, and not to perform a clinical study or evaluate the yield of the manufactured biochip devices (Supplementary Note 7). As a general guideline, experiments with synthetic DNA targets or commercially available cultured samples were performed ≥ 3 times. Tests with patient samples were conducted once. In all CMOS biochip, ≥ 5 identical IFT probe replicate were used. The statistical details and number of replicate for each experiment are included in Supplementary Notes 11-12.

2. Data exclusions

Describe any data exclusions.

Any data, including physical, bio-physical, chemical, or biological extracted from any biochip or its components that failed to pass internal QC tests has been excluded. Our internal QC tests check/verify CMOS chip electrical/optical functionality (failure frequency < %1), surface functionalization and probe printing (failure frequency < 2%), biochip module assembly and fluidics integrity (failure frequency = 7%), and the NA extraction and NAAT amplification chemistry (failure < 3%).

NOTE: The above failure rates are estimations from early 2017, when the patient samples were tested on the prototype systems. These numbers, except CMOS biochip electrical/optical and surface functionalization failure rates, have been improved since then as our product development has progressed.

3. Replication

Describe whether the experimental findings were reliably reproduced.

Yes, the results were reliably reproduced.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

All experiments were done using randomly selected CMOS biochip devices without any pre-selection or sorting. Blind experiment were done for 11 patient samples. The other proof-of-principle experiments were done with known and prepared and qualified samples.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

The upper respiratory panel validation experiments using patient samples were done in a blinded fashion, i.e., the team members responsible for the biochip experiments and its data analysis were not aware of the results from the GenMark system. Once they made the determinations regarding the presence of a pathogen for all 11 experiments, they were made aware of the GenMark system results.

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

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6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

n/a	Confirmed
☐	☒ The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.)
☐	☒ A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒ A statement indicating how many times each experiment was replicated
☒	☐ The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section)
☐	☒ A description of any assumptions or corrections, such as an adjustment for multiple comparisons
☒	☐ The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted
☐	☒ A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range)
☐	☒ Clearly defined error bars

See the web collection on statistics for biologists for further resources and guidance.

Software

Policy information about availability of computer code

7. Software

Describe the software used to analyze the data in this study.

Bioinformatics: PERL version 5.20.2. DNASoftware: Visual Oligonucleotide Modeling Platform (VISUALOMP) version 3.7.0.5113 and Oligonucleotide Modeling Platform Developer Edition 2015. PCB Design: Orcad Capture version 16.5. Data Analysis: MATLAB version R2015a. Circuit Design: Cadence Virtuoso Product Suite version 6.1.

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

Materials and reagents

Policy information about availability of materials

8. Materials availability

Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company.

1. The NAAT reagents used in the platform, including the amplification master mix, primers and probes are all available from for-profit commercial entities. The names of all the commercial entities are listed in the Supplementary Information section.

2. The biochip module, including the CMOS chip and the associated reader electronics are product prototypes of InSilixa, Inc. At this point in time, there are practical limitations for the broad availability as they are in the product development phase.

3. The M. Tuberculosis samples and strains, specifically the drug-resistant strains tested in the study, are available for distribution with some practical restrictions from "Institute of Tropical Medicine, Antwerp, Belgium".

4. The anonymous patient remnant samples used in the upper respiratory panel validation experiments are from "Stanford University Clinical Virology Lab", courtesy of Prof. Benjamin A. Pinsky. There are no restrictions on the availability or use of these archived remnant samples except by consent of Prof. Pinsky.

9. Antibodies

Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species).

No antibodies were used in this study.

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10. Eukaryotic cell lines

a. State the source of each eukaryotic cell line used. — No eukaryotic cell lines were used in this study.

b. Describe the method of cell line authentication used. — No eukaryotic cell lines were used in this study.

c. Report whether the cell lines were tested for mycoplasma contamination. — No eukaryotic cell lines were used in this study.

d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use. — No eukaryotic cell lines were used in this study.

Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

Provide details on animals and/or animal-derived materials used in the study. — No animals were used in this study.

Policy information about studies involving human research participants

12. Description of human research participants

Describe the covariate-relevant population characteristics of the human research participants. — The patient samples were anonymous, archived remnant samples. We have no information regarding population characteristics of the patients, only prior test results.

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